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Amendments to the Substitute Specification:

Replace the paragraph beginning at line 14 on page 38 with the following amended paragraph:

A non-limiting example of how peptide inhibitors of the B1 interaction with other proteins via its prodomain or kinase domain, as noted above, would be designed and screened is based on previous studies on peptide inhibitors of ICE or ICE-like proteases, the substrate specificity of ICE and strategies for epitope analysis using peptide synthesis. The minimum requirement for efficient cleavage of a peptide by ICE was found to involve four amino acids to the left of the cleavage site with a strong preference for aspartic acid in the P₁ position and with methylamine being sufficient to the right of the P₁ position (Sleath et al., 1990; Howard et al., 1991; Thornberry et al., 1992). Furthermore, the fluorogenic substrate peptide (a tetrapeptide), acetyl-Asp-Glu-Val-Asp-a-(4-methyl-coumaryl-7-amide) (SEQ ID NO:3) abbreviated Ac-DEVD-AMC, corresponds to a sequence in poly (ADP-ribose) polymerase (PARP) found to be cleaved in cells shortly after FAS-R stimulation, as well as other apoptopicapoptotic processes (Kaufmann, 1989; Kaufmann et al., 1993; Lazebnik et al., 1994), and is cleaved effectively by CPP32 (a member of the CED3/ICE protease family) and MACH proteases.

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Following page 64, please insert references 53-75 as follows:

- 53. Ruzicka et al., (1993) Science 260, 487.
- 54. Sambrook et al. (1989) Molecular cloning: a laboratory manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.
- 55. Sano et al., (1992) Science 258, 120.
- 56. Sano et al., (1991) Biotechniques 9, 1378.
- 57. Schreiber, E., Matthias, P., Muller, M.M. and Schaffner,
- W. (1989), Nuc. Acids Res. 17:6419.
- 58. Schulz et al., G.E., Principles of Protein Structure, Springer-Verlag, New York, N.Y. 1798.
- 59. Sleath, P.R. et al. (1990) J. Biol. Chem. 265,14526-14528.
- 60. Smith, C. A., Farrah, T., and Goodwin, R. G. (1994). Cell 76, 959-962.
- 61. Stanger, B.Z. et al. (1995) Cell 81, 513-523.
- 62. Thornberry, N.A. et al. (1992) Nature 356,768-774.
- 63. Thornberry, N.A. et al. (1994) Biochemistry 33, 3934-3940.
- 64. Uren, A.G. et al. (1996) Proc. Natl. Acad. Sci USA 93, 4974-4978.
- 65. Vandenabeele, P., Declercq, W., Beyaert, R., and Fiers, W. (1995). Trends Cell Biol. 5, 392-400.

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- 66. Varfolomeev, E. E., Boldin, M. P., Goncharov, T. M., and Wallach, D. (1996) J. Exp. Med. in press.
- 67. Vassalli, P. (1992) Ann. Rev. Immunol. 10, 411-452.
- 68. Veira et al., (1987) Meth. Enzymol. 153, 3.
- 69. Wallach, D. (1996) Eur. Cytokine Net. 7, 713-724.
- 70. Wallach, D. (1997) Trends Biochem. Sci. 22, 107-109.
- 71. Wang, L. et al. (1994) Cell 78, 739-750.
- 72. Wilks, A.F. et al. (1989) Proc. Natl. Acad. Sci. USA, 86:1603-1607.
- 73. Yang, E. and Korsmeyer, J. (1996) Blood 88(2), 386-401.
- 74. Zaccharia, S. et al. (1991) Eur. J. Pharmacol. 203, 353-357.
- 75. Zhao, J.J. and Pick, L. (1993) Nature 365: 448-451.